REMARKS

Applicants wish to express their appreciation for the court ices extended to the undersigned attorney and inventor Dr. Thomas Webster during a telephonic interview conducted on April 15, 2010. The Examiner's interview summary accurately describes the content of that discussion. In particular, during that conversation applications discussed the compositions of Yadav et al (US Patent No. 6,572,672) and the differences between the compositions disclosed in Yadav and applications claimed compositions. Applicants emphasized that when fabricating a consolidated composition from nanoparticles the conditions used during the formation process must be carefully controlled to produce a final structure that has nanoscale dimensions, including for example nanosized particles and surface roughness. Therefore in spite of the fact that Yadav prepares their compositions using nanoparticle starting materials, due to particle agglomeration, the final product will not necessarily have a particle size less than 500 nanometers. Applicants stated they would submit an affidavit confirming these statements.

Claims 1, 11 and 12 are amended to explicitly recite that the present compositions are compositions comprising consolidated nanoparticles. Support for that amendment is found in the last sentence of page 3. Claim 12 has been further amended to specify the final composition has a particle size between 200 and 500 nanometers and a surface roughness between about 11 and 360 nanometers root mean square. Support for the amendments is found throughout the specification including for example in paragraph [0008] beginning at the bottom of page 2 of the specification.

Claims 1-4, 8-11 and 13-15 stand rejected under 35 USC 103 as being obvious over the teachings of Yadav et al (US patent no. 6,572,672). Applicants respectfully traverse this rejection.

The present invention is directed to compositions that are formed from metal starting materials under controlled conditions to provide a final composition that comprised of nanoparticles and having a surface roughness of less than 500 nanometers root mean square.

The Examiner has cited the Yadav reference as disclosing the use of nanostructured substances in orthopedic applications. In particular, in one disclosed embodiment, Yadav teaches the formation of consolidated materials formed by compressing the nanostructured

starting materials. The Examiner contends that the consolidated materials formed in such a process must inherently have applicants claimed particle size and surface roughness. However, applicants note that the final material prepared in accordance with Yadav does not necessarily have the same surface features as the starting nanostructured powder.

Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient (*In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)). "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)

As stated in the accompanying 37 CFR 1.132 Declaration by Dr. Thomas Webster, the conditions used during the process of forming a consolidated material from metal powder must be carefully controlled if the end product is desired to have nanoscale dimensions. Absent a careful formation process, agglomeration of the individual particles will occur resulting in a final composition having significantly larger dimensions (e.g., in the micron range) than the starting material.

Applicants have made the surprising discovery that osteoblast adhesion at the metal/tissue interface can be increased by utilizing metals the exhibit nano-particle and nano-surface roughness. More particularly, metals having nanosized particles of less than 500 nm and a surface roughness between 11 and 360 nm rms display an enhanced level of osteoblast adhesion (see paragraph [00015] and [00016] of the application as filed) relative to standard materials. Yadav et al is devoid of any teaching or suggestion regarding the preparation of consolidated materials that display surface roughness of less than 500 nm rms and/or comprise nanoparticles of less than 500 nm. Furthermore, Yadav fails to appreciate that consolidated materials exhibiting nanosized dimensions have superior properties with regards to orthopedic applications. Accordingly, Yadav fails to provide motivation to modify their procedures to allow for the formation of consolidated materials exhibiting nanosized dimensions.

Applicants have surprisingly found that consolidated materials can be formed using metal nanoparticles as the starting material in the absence of binders and at room temperature and using relatively low pressures (5-10 gigapascals). The resulting consolidated materials have particle sizes of less than 500 nm and a surface roughness of less than 500 nm.

Yadav teaches the use of binders and sintering temperatures for the formation of their consolidated compositions. In each of the examples, and throughout the specification, when Yadav discloses pressing the powders to form as consolidated material, the material is either sintered or is combined with a binder prior to compression. For example, in Example 8 which is the only example directed to biomedical products Yadav teaches, "To prepare an orthopedic implant, the synthesized powders are uniaxially pressed. Poly(ethylene glycol) (PEG) may be used as a binder for compaction of the powders. PEG is added to the powders by preparing a 1 weight percent solution in ethanol and wet mixing the solution with the alloyed powders."

As noted in the accompanying 37 CFR 1.132 Declaration by Dr. Thomas Webster, the use of high temperatures (sintering) or the use of binders increases agglomeration, leading to a final composition that has an increase particle size and increase surface roughness at the micron scale. Presumably, Yadav thought that sintering and/or use of binders were necessary to hold the consolidated material together. Thus not only did Yadav fail to provide any motivation for forming the consolidated compositions of the present invention, Yadav also failed to teach how to prepare consolidated compositions having nanoscale dimensions.

Yadav et al discloses forming metallic orthopedic devices from powders having grain sizes less than 500 nm. However, the reference is devoid of any teaching or suggestion regarding the desired surface roughness or the particle size of the final compositions. Claim 1 of the present invention as amended herein requires the biomaterial to be comprised of consolidated nanoparticles, wherein the final consolidated material not only has a particle size of less than 500 nm, but also has a surface roughness of less than about 500 nanometers root mean square (nm rms).

Applicants respectfully submit that surface roughness is not necessarily directly correlated with grain size. Accordingly, even if for the sake of argument the disclosed metallic material of Yadav et al, is formed under conditions allowing the composition to comprise nano-sized grains (which applications respectfully submit will not happen under sintering conditions or with use of a binder), the material so formed does not inherently have a surface roughness of less than about 500 nm rms. As shown in the Woodcock et al, reference submitted with applicants' response dated August 12, 2010, materials having similar grain sizes can produce different surface roughness based on the orientation of the grains. In particular, see Figure 6 of Woodcock which shows the same grain sizes oriented in a different manner comparing the left to the right of the AFM image. On the right, the grains are perpendicular (sticking out) and on the left they are parallel to the surface. The paper goes

on to say (as can be clearly seen) that these two different regions on the AFM have different roughness. Applicants claimed compositions require both the particle size and the surface roughness to be less than 500 nm.

The Yadav reference is devoid of any teaching or suggestion with regards to particle size and/or surface roughness in the final consolidated materials. Furthermore, the reference fails to suggest that altering the particle size or surface roughness of a metal to nano-sized proportions would improve osteoblast adhesion to such a surface. Applicants have described a novel biomaterial that exhibits unexpected properties (e.g., enhanced osteoblast adhesion). Accordingly, the claimed invention is believed to be patentably distinct over the teachings of Yadav et al., and applicants respectfully request the withdrawal of the rejection of claims 1-4, 8-11 and 13-15 as being obvious over the teachings of Yadav et al (US patent no. 6,572,672).

Claims 5-6 stand rejected under 35 USC 103 as being obvious over the combined teachings of Yadav in view of Oshida (US Patent no. 6,183,255). Applicants respectfully traverse this rejection.

The deficiencies of the Yadav disclosure with regards to the claimed invention have been discussed above. Claims 5 and 6 ultimately depend from claim 1 and thus incorporate all the limitations of the base claim. The secondary Oshida reference fails to supplement the deficiencies of the Yadav reference with regards to the disclosed use of materials that have a surface roughness of less than 500 nm rms and/or are comprised of particles having a size of less than 500 nanometers. Accordingly, the combined teachings of Yadav and Oshida fail to teach or suggest the present invention. The invention of claims 5 and 6 is believed to be patentably distinct over the teachings of those references and applicants respectfully request the withdrawal of the rejection of claims 5 and 6 for obviousness.

Claim 7 stands rejected under 35 USC 103 as being obvious over the combined teachings of Yadav in view of Davidson (US Patent no. 5,415,704). Applicants respectfully traverse this rejection.

The deficiencies of the Yadav disclosure with regards to the claimed invention have been discussed above. Claim 7 depends from claim 1 and thus incorporates all the limitations of the base claim. The secondary Davidson reference fails to supplement the deficiencies of the Yadav reference with regards to the disclosed use of materials that have a surface roughness of less than 500 nm rms or are comprised of particles having a size of less than 500 nanometers. Accordingly, the combined teachings of Yadav and Davidson fail to teach or

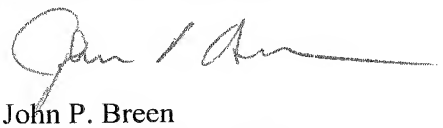
suggest the present invention. The invention of claim 7 is believed to be patentably distinct over the teachings of those references and applicants respectfully request the withdrawal of the rejection of claim 7 for obviousness.

Claim 16 stands rejected under 35 USC 103 as being obvious over the combined teachings of Yadav in view of Davidson (US Patent no. 5,415,704). Applicants respectfully traverse this rejection.

The deficiencies of the Yadav disclosure with regards to the claimed invention have been discussed above. Claim 16 depends from claim 13 and thus incorporates all the limitations of the base claim. The secondary Davidson reference fails to supplement the deficiencies of the Yadav reference with regards to the disclosed use of materials that have a surface roughness of about 11 to 360 nm rms and are comprised of particles having a size of about 200 to 500 nanometers. Accordingly, the combined teachings of Yadav and Davidson fail to teach or suggest the present invention. The invention of claim 16 is believed to be patentably distinct over the teachings of those references and applicants respectfully request the withdrawal of the rejection of claim 16 for obviousness.

Claimed invention as amended herein is believed to be patentable over the combined teaching of the cited prior art. Accordingly, applicants respectfully request allowance of the claims, and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,



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